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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,474	04/12/2006	Hiroko Kojima	062405	3422

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EXAMINER	
SHEN, WU CHENG WINSTON	

ART UNIT	PAPER NUMBER
1632	

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06/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,474	KOJIMA ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-12 and 14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 25, 2008 has been entered.

Claims 9-12 and 14-23 are pending in the instant application. Claim 13 is cancelled. Claims 9, 11, and 12 are amended. Claims 14-23 are newly added. Claims 9-12 and 14-23 are currently under examination.

This application 10/575,474 filed on 04/12/2006 is a 371 of PCT/JP04/15673 filed on 10/15/2004 and claims the priority of foreign application JAPAN 2003-355505 filed on 10/15/2003.

Claim Objections

2. Claims 9 and 17 are objected because of the following informalities: (i) claims 9 and 17 recites the phrase "osteo-inducible transcription factor Cbfa1", which should read as "osteo-inducing transcription factor Cbfa1" because as written "osteo-inducible" modifies a characteristic of Cbfa1 such that it is induced by "osteo". Osteo-inducing means Cbfa1 induces an "osteo" fate or "osteo" genes; and (ii) claims 9 and 17 recites the phrase "vector carrying a gene encoding", and the phrase more precise if written as "vector comprising a gene encoding".

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Previous rejection of claims 9-12 under 35 U.S.C. 102(e) and under 35 U.S.C. 102(a) as being anticipated by Kumta et al. (Kumta et al., U.S Patent application Publication 2003/0219466, Publication date, Nov. 27, 2003, filed on Mar. 19, 2003), is ***withdrawn*** in light of Applicant's arguments, which are found persuasive. The withdrawal of this rejection has been documented in the advisory action dated 02/26/2008.

4. Previous rejection of Claims 9-12 under 35 U.S.C. 102(e) and under 35 U.S.C. 102(a) as being anticipated by Doll et al. (Doll et al., U.S Patent application Publication 2003/0235564, Publication date, Dec. 25, 2003, filed on May 13, 2003) is ***withdrawn*** in light of Applicant's arguments that the rejection does not address adsorption of Runx2 by bioadaptable porous material (including β-TCP, tricalcium phosphate) can occur inherently when Runx2, water and β-TCP are mixed together.

However, the following new rejection is necessitated by claim amendments in combination of Applicant's arguments filed on 03/25/2008.

5. Claims 9-12 and 14-23 are newly rejected under 35 U.S.C. 102(e) and under 35 U.S.C. 102(a) as being anticipated by **Doll et al.** (Doll et al., U.S Patent application Publication 2003/0235564, Publication date, Dec. 25, 2003, filed on May 13, 2003) as evidenced by **Ogawa et al.** (US patent 5,030,611, issued 07/09/1991).

Independent claims 9 and 17 are directed to a bioadaptable porous material on which an adenoviral or retroviral vector carrying a gene encoding an osteo-inducible transcription factor Cbfal is adsorbed, wherein the bioadaptable porous material is any member selected from the group consisting of α-TCP, β-TCP (tricalcium phosphate), collagen, polylactic acid, hyaluronic acid, polyglycolic acid, and a complex of any thereof. Dependent claims recite limitation further comprising bone marrow derived cells that are osteoblasts.

Claim interpretation: Bone marrow derived cells, including osteoblasts, recited in newly added claims 14-16 and 21-23 read on bone marrow derived cells that are not transfected, and bone marrow derived cells that are transfected with any viral vector encoding any gene of interest. In other words, claims 14-16 and 21-23 read on addition of non-recombinant bone marrow derived cells to the implant as well as bone marrow derived cells that are transformed with the gene recited in claim 9. The limitation "an individual in need of said implant" recited in claims 16 and 23 reads on any individual.

With regard to Cbfa1 recited in independent claims 9 and 17 of instant application, Doll et al. teaches transcription factor Runx2, also referred to as Cbfa1 (core binding factor alpha 1) and as Osf2 (osteoblast specific factor 2), which is a regulator of osteoblast differentiation (See parag. [0022], column 3, Doll et al. 2003).

Doll et al. teach a pharmaceutical composition comprising in combination the Runx2 protein, a polynucleotide encoding the Runx2 protein, or a cell that has been transformed with a polynucleotide encoding Runx2 protein, in a pharmaceutically acceptable carrier (which includes water, buffer, saline etc), the carrier comprising a bio-compatible, biodegradable polymeric matrix. Another aspect of the invention includes a device comprising the above-described pharmaceutical composition in combination with a sterile and substantially antigen-free, pre-shaped allograft or xenograft bone implant (See abstract, Doll et al., 2003).

With regard to an implant consisting of a bioadaptable material and its association with DNA (claims 9-12 and 17-20 of instant application), Doll et al. teach a method for repairing a bone defect comprising administering to a mammalian patient at the site in need of treatment a pharmaceutical composition, comprising in combination the Runx2 protein, a polynucleotide encoding the Runx2 protein, or a cell that has been transformed with *a polynucleotide encoding Runx2 protein*, in a pharmaceutically acceptable carrier wherein the carrier is a bio-compatible, biodegradable polymeric matrix (See abstract, Doll et al., 2003). Doll et al. teach viral vectors have higher transaction (ability to introduce genes) abilities than do most chemical or physical methods to introduce genes into cells. And the viral vectors include retroviral vectors and adenoviral vectors (See parag. [0096], [0097], and [0098], Doll et al., 2003).

With regard to β-TCP (β-tricalcium phosphate) (claims 10-12 and 17-20 of instant application), Doll et al. teach the reports on the use of β-tricalcium phosphate for implantation; and reports on the use of demineralized bone implants (See parag. [0053], column 7, Doll et al., 2003).

The inherent properties of β-TCP to adsorb nucleic acids and/or proteins are known in the art. For instance, Ogawa et al. teaches packing tricalcium phosphate (TCP) or hydroxyapatite for chromatography, and TCP exhibits a high ability to adsorb acidic proteins and nucleic acid (See for instance, lines 54-59, 28-33, column 4, Ogawa et al., 1991).

With regard to the implant further comprising bone marrow derived cells such as osteoblasts (claims 14-16 and 21-23 of instant application), Doll et al. teaches examples for bone repair and/or treatment of osteoporosis uses osteocytes/osteoblasts transfected with bone growth factor genes (See paragraph [0115], Doll et al., 2003). Doll et al. further teaches combination of a form of Runx2 with a delivery system (which reads on a cell such as osteoblasts) that comprises biologically active molecule, which enhances the rate of bone repair (See paragraph [0116], Doll et al., 2003).

Thus, Doll et al. clearly anticipates claims 9-12 and 14-23 of instant invention.

Applicant's arguments

Applicant's remarks regarding the previous rejection of record are addressed as the related to the new grounds of rejection set forth above. With regard to whether Doll et al. anticipates claims of instant application, Applicant argues that Doll is silent with respect to how the Runx2 plasmid is incorporated into a bioadaptable material. However, Applicant argues Doll

describes at paragraph [0067] that:

injecting a suspension of cells in a polymer solution improves the reproducibility of cell seeding throughout a device, and protects the cells from shear forces or pressure induced necrosis, and aids in defining the spatial location of cell delivery. Applicant argues that, based on the disclosure of paragraph [0067] of Doll et al., the cells are subjected to a high pressure during the course of incorporating the Runx2 into the porous material. Applicant concludes that as such, adsorption cannot occur.

Response to Applicant's arguments

TCP exhibits a high ability to adsorb acidic proteins and nucleic acid (See for instance, lines 54-59, 28-33, column 4, Ogawa et al., 1991) has been discussed in the rejection anticipated by Doll et al. as evidenced by Ogawa et al.

The Examiner agrees that Doll et al. does not explicitly describe the process how the Runx2 plasmid is incorporated into a bioadaptable material such as TCP. However, TCP exhibiting a high ability to adsorb acidic proteins and nucleic acid is well known in the art. It is worth noting that the claims do not recite any specific condition (low pressure, degasified, for instance) how adsorption occurs. Therefore, the teachings by Doll on a pharmaceutical composition comprises β-TCP and a polynucleotide encoding Cbfa1 in a pharmaceutically accepted carrier (which reads water, buffer, saline etc) inherently anticipate the claimed adsorption of th4e nucleic acid by the β-TCP.

The Examiner notes that the Application's interpretation of paragraph [0067] is taken out of context of Doll et al. The sentences before and after the citation by Applicant (underlined) are provided below.

[0067] Another pharmaceutically acceptable carrier for use in the pharmaceutical composition, device and method of the present invention is a biocompatible and biodegradable polymer which forms a hydrogel. Polymers that form ionic hydrogels, which are malleable, are suitable carriers for Runx2, either in protein, nucleic acid or transformed cellular form. Furthermore, injecting a suspension of cells in a polymer solution improves the reproducibility of cell seeding throughout a device, and protects the cells from shear forces or pressure induced necrosis, and aids in defining the spatial location of cell delivery. The injectable polymer is also utilized to deliver cells and promote the formation of new tissue without the use of any other matrix.

In this paragraph, Doll et al. discusses the embodiment of using cells as carrier of Runx2 by transforming/transfecting the nucleic acid encoding Runx2 into the cells. And the integrity of the cells can be protected from shear forces or pressure upon injection to a site where repair is needed by having the cells suspended in biocompatible and biodegradable polymer which forms a hydrogel. Nowhere does Doll et al. disclose in this paragraph a high pressure during the course of incorporating the Runx2 into the porous material, and as such, adsorption cannot occur.

Conclusion

6. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30

PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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